Claims

1. A method for inducing an immune response to latent tuberculosis in an individual, said method comprising the step of delivering a composition comprising one or more polypeptides or fragments thereof, which polypeptides are upregulated or expressed during the latent stage of the mycobacteria infection, and/or nucleic acids encoding these polypeptides.

2. The method according to claim 1, wherein said individual is infected by a virulent mycobacterium, e.g. *M. tuberculosis*, and is not vaccinated with BCG against tuberculosis.

3. The method according to claim 1, where the polypeptides upregulated during the latent stage of the mycobacteria infection, comprises one or more an amino acid sequences selected from

    (a) SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 ,21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44 and 45

    (b) an immunogenic portion, e.g. a T-cell epitope, of any one of the sequences in (a); and /or

    (c) an amino acid sequence analogue having at least 70% sequence identity to any one of the sequences in (a) or (b) and at the same time being immunogenic.

4. The method according to claim 3, where the immunogenic portions are selected from the group consisting of SEQ ID NO 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44 and 45.

5. The method according to claim 1, where the nucleic acid sequences are selected from SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53 ,54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89 and 90.

6. A therapeutic vaccine against tuberculosis comprising one or more polypeptides or fragments hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection, and/or nucleic acids encoding these polypeptides.

7. A therapeutic vaccine according to claim 6 where the polypeptides upregulated during the latent stage of the mycobacteria infection, which stage is characterized by low-oxygen tension in the microenvironment of the mycobacteria, comprises one or more amino acid sequences selected from

(a)   SEQ ID NO 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44 and 45

(b)   an immunogenic portion, e.g. a T-cell epitope, of any one of the sequences in (a); and /or

(c)   an amino acid sequence analogue having at least 70% sequence identity to any one of the sequences in (a) or (b) and at the same time being immuno-genic.

8. A therapeutic vaccine according to claim 7, where the immunogenic portions are selected from the group consisting of SEQ ID NO 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 ,21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44 and 45.

9. A therapeutic vaccine according to claim 6, where the polypeptides or fragments hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection, which stage is characterized by low-oxygen tension in the microenviron-ment of the mycobacteria, are fused to other antigens expressed by bacteria within the mycobacteria family.

10. A therapeutic vaccine according to claim 9 where the fusion partners is selected from the group consisting of ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19kDa lipoprotein, MPT32.

11. A therapeutic vaccine according to claims 6, where the nucleic acid sequence are selected from SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53 ,54, 55, 56, 57, 58, 59, 60,

61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89 and 90.

12. A multiphase vaccine comprising antigen components with therapeutic activity according to claim 6 combined with antigen components with prophylactic activity.

13. A multiphase vaccine according to claim 12 where the antigen components with prophylactic activity comprises ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19kDa lipoprotein or MPT32.

14. A vaccine according to claim 6, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a DNA fragment comprising an antigen component with therapeutic activity selected from SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53 ,54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89 and 90 or/and an antigen component with prophylactic activity has been incorporated into the genome of the microorganism in a manner allowing the microorganism to express and optionally secrete the polypeptide.

15. A vaccine according to claim 14 where the non-pathogenic microorganism is selected among bacteria or virus.

16. A vaccine according to claim 6, where the antigen components are recombinant polypeptides or synthetic peptides delivered in a delivery system such as an adjuvant.

17. A vaccine according to claims 6 in which the amino acid sequence is lipidated so as to allow a self-adjuvanting effect of the polypeptide.

18. A method for treating an animal, including a human being, with tuberculosis caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the vaccine according to claim 6.

19. A method for immunizing an animal, including a human being, against tuberculo-
sis caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis, Mycobacte-
rium africanum* or *Mycobacterium bovis*, comprising administering to the animal the
vaccine according to claim 12.

20. A method of diagnosing tuberculosis caused by virulent mycobacteria, e.g. by
Mycobacterium tuberculosis, Mycobacterium africanum or *Mycobacterium bovis*, in
an animal, including a human being, comprising application or intradermally injecting,
in the animal, polypeptides or fragments hereof, which polypeptides are expressed
during the latent stage of the mycobacteria infection, and/or nucleic acids encoding
these polypeptides, a positive skin response at the location of injection or application
being indicative of the animal having tuberculosis, and a negative skin response at
the location of injection or application being indicative of the animal not having tuber-
culosis.

21. A method for diagnosing previous or ongoing infection with a virulent mycobacte-
rium, said method comprising contacting a sample, e.g. a blood sample, comprising
mononuclear cells (e.g. T-lymphocytes), with a polypeptides or fragments hereof,
which polypeptides are expressed during the latent stage of the mycobacteria infec-
tion, which stage is characterized by low-oxygen tension in the microenvironment of
the mycobacteria, in order to detect a positive reaction, e.g. proliferation of the cells
or release of cytokines such as IFN-γ.

22. A method of diagnosing *Mycobacterium tuberculosis* infection in a subject
comprising:

(a)   contacting a polypeptides or fragments hereof, which polypeptides are ex-
        pressed during the latent stage of the mycobacteria infection, which stage is
        characterized by low-oxygen tension in the microenvironment of the myco-
        bacteria, with a bodily fluid of the subject;

(b)   detecting binding of an antibody to said polypeptide, said binding being an
        indication that said subject is infected by *Mycobacterium tuberculosis* or is
        susceptible to *Mycobacterium tuberculosis* infection.